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Synthesis of the Lignin Model Compounds *Threo*-Guaiacylglycerol-β-Guaiacyl Ether and *Threo*-Veratrylglycerol-β-Guaiacyl Ether

By John Ralph and Raymond A. Young

Department of Forestry, University of Wisconsin Madison, Wisconsin 53706 U.S.A.

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^{13}C NMR
^{1}H NMR

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Summary

The lignin model compounds guaiacylglycerol-β-guaiacyl ether and veratrylglycerol-β-guaiacyl ether are produced predominantly in the *threo* form by lithium tri-*sec*-butylborohydride reduction of the corresponding α-ketones. Previously published syntheses yield predominantly the *erythro* isomer.

Kurzmitteilung

Schlüsselwörter (Sachgebiete)
Lignin-Modellverbindungen
^{13}C NMR
^{1}H NMR

Synthese der Lignin-Modellverbindungen threo-Guajacylglycerin-β-Guajacylether und threo-Veratrylglycerin-β-Guajacylether

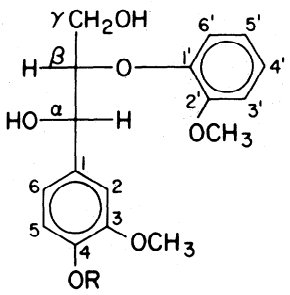
Zusammenfassung

Die Lignin-Modellverbindungen Guajacylglycerin-β-Guajacylether und Veratrylglycerin-β-Guajacylether werden vorzugsweise in der *threo* Form durch Lithium-tri-sec-Butylborhydrid – Reduktion der entsprechenden α-Ketone gebildet. Früher veröffentlichte Synthesen ergaben vorzugsweise das Erythro-*isomer.*

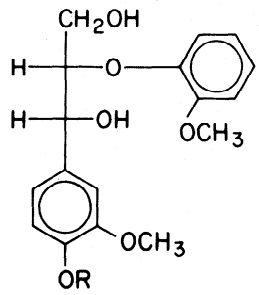
β-Aryl ether models are commonly employed for investigation of lignin reactions. In the case of the phenylpropanoid models, guaiacylglycerol-β-guaiacyl ether [1-(3-methoxy-4-hydroxyphenyl)-2-(2-methoxyphenoxy)-propan-1,3-diol], and veratrylglycerol-β-guaiacyl ether [1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-propan-1,3-diol], stereoisomeric effects are often neglected. Alternatively the results are compared between reactions run firstly with the *erythro* isomer 2a or 2c, prepared by the method of Nakatsubo et al. (1975), Berndtsson and Lundquist (1977) or Miksche et al. (1966), and seondly with a mixture of *threo* and *erythro* isomers. It is therefore of interest to obtain a facile synthesis of the *threo* isomer for comparative studies.

L-Selectride (lithium tri-*sec*-butylborohydride, 2.1 equivalents) reduction of the ketones 3b, 3c at −78 °C in THF followed by oxidative workup produced the required alcohols in essentially quantitative yield, predominantly in the *threo* form (1b:2b > 80:20, 1c:2c > 85:15, estimated from 270 MHz NMR of the diacetates or triacetates). This represents a reversal in selectivity, $LiAlH_4$ (for example) yielding largely the *erythro* isomer (ca. 75:25, 2b:1b). Compound 1a, the free phenolic model in which most of our interest lies, was crystallized from diethyl ether once seed crystals were available. Further crystallization from ethyl acetate/hexane was possible until the mother liquor reached about 30:70 1b:2b, representing crystallization of approximately 70% of the total product as the *threo* isomer. At this point, seeding the mother liquor with a crystal of the *erythro* isomer produced a small crop of *erythro* crystals.

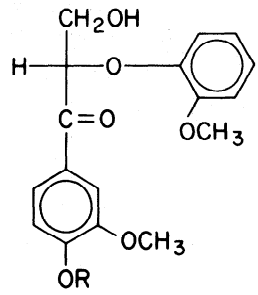
This scheme complements the synthesis of the *erythro* isomers 2a and 2c by Nakatsubo et al. (1975) and has the advantage of a higher yield of crystalline product. Also a wide variety of commonly used β-aryl ether lignin models are traditionally synthesized from the immediate precursor to 3, namely 4 (Kratzl et al. 1959).



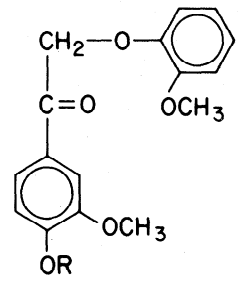
1



2



3



4

a. R = H
b. R = $CH_2\Phi$
c. R = CH_3

L-Selectride Reduction Procedure

Ketones 3 were prepared by methods similar to Kratzl et al. (1959) and, more recently, Landucci et al. (1981). L-Selectride (lithium tri-*sec*-butylborohydride) was obtained from Aldrich Chemical Company as a 1M solution in THF. The ketone 3b (6.00 g, 14.71 mmole) was dissolved in THF (150 ml, dried and freshly distilled over sodium) under nitrogen, with stirring, and cooled to −78 °C. L-Selectride (1M in THF, 33 ml, 33 mmole) was added dropwise over a period of 20 minutes while stirring at −78 °C. Stirring was continued for 6–7 hours at −78 °C and the reaction mixture allowed to slowly warm to room temperature (overnight) with continued stirring. The borane was oxidized using 3N NaOH (20 ml) and 30% H_2O_2 (20 ml) and the mixture refluxed for 1 hr. The product was then extracted into diethyl ether, washed 3–4 times with saturated aqueous K_2CO_3, then with saturated aqueous NaCl twice. The organic phase was dried over $MgSO_4$ and evaporated to dryness to give a virtually quantitative yield (≥ 98%, of the α-alcohol as a mixture of isomers 1b:2b in the approximate ratio 80:20, estimated subsequently form 270 MHz ^{1}H NMR of the triacetates of 1a, 2a).

Debenzylation with 5% Pd/C, 1 atm H_2, at room temperature overnight in wet THF or 95% ethanol gives the required free phenolic products 1a:2a in virtually quantitative yield.

Spectral Data

Compound 1a *(Threo)*: White needles, mp 119.5–120 °C

IR (KBr Disk) 3440, 2950, 2850, 1600, 1520, 1510, 1460, 1440, 1280, 1260, 1220, 1180, 1160, 1130, 1030, 770, 750 cm^{-1}

^{1}H NMR (100 MHz, $CDCl_3$) δ 3.5–4.0 (m, 2H, γHs), 3.81 and 3.86 (2 s, 6H, methoxyls), 4.08 (m, 1H, H_β), 4.99 (d, J = 7.7 Hz, 1H, H_α), 6.1 (bs, 1H, phenolic hydroxyl), 6.7–7.2 (m, 7H, aromatics)

^{13}C NMR (15.0 MHz, $CDCl_3$) δ 55.9 (methoxyls), 61.1 (Cγ), 74.0 (C_α), 89.1 (C_β); 131.6, 109.6, 146.7, 145.6, 114.4, 120.2 (C_1–C_6, respectively); 151.2, 147.3, 112.2, 124.0, 121.7, 120.7 (C_1'–C_6', respectively).

Triacetate of 1a: White crystalline solid, mp = 93.5–94 °C

^{1}H NMR (270 MHz, $CDCl_3$) δ 2.00, 2.05, 2.29 (3 s, 9H, acetate methyls), 3.81 (2 s, 6H, methoxyls); ABMX pattern, A = $H\gamma_1$, B = $H\gamma_2$, M = H_β, X = H_α; ν_A = 4.06, ν_B = 4.32, ν_M = 4.63, ν_X = 6.13, J_{AB} = 11.95 Hz, J_{AM} = 5.71 Hz, J_{BM} = 4.59 Hz, J_{MX} = 6.43 Hz; 6.8–7.1 (m, 7H, aromatics)

^{13}C NMR (15.0 MHz, $CDCl_3$) δ 20.5, 20.5, 20.9 (acetate methyls), 55.9 (methoxyls), 63.1 (C_γ), 74.6 (C_α), 80.2 (C_β)

Compound 1c *(Threo)*: Colorless oil

^{1}H NMR (60 MHz, $CDCl_3$) δ 3.0 (bs. 2H, OH's), 3.4–4.3 (m 3H, Hγ's and H_β), 3.83 (3 s, 9H, methoxyls), 4.95 (d, J = 7.5 Hz, 1H, H_α), 6.8–7.2 (m, 7H, aromatics)

^{13}C NMR (15.0 MHz, $CDCl_3$) δ 55.9 (methoxyls), 61.1 (C_γ), 73.8 (C_α), 88.7 (C_β)

Diacetate of 1c

^{1}H NMR (270 MHz, $CDCl_3$) δ 2.01 and 2.02 (2 s, 6H, acetate methyls), 3.83, 3.86, and 3.87 (3 s, 9H, methoxyls), ABMX pattern, A = $H\gamma_1$, B = $H\gamma_2$, M = H_β, X = H_α; ν_A = 4.01, ν_B = 4.28, ν_M = 4.64, ν_X = 6.08, J_{AB} = 11.76 Hz, J_{AM} = 5.90 Hz, J_{BM} = 4.03 Hz, J_{MX} = 6.62 Hz; 6.8–7.0 (m, 7H, aromatics)

Compound 2a *(Erythro)*: White needles, mp 94–95 °C

^{1}H NMR (100 MHz, $CDCl_3$) δ 3.5–4.0 (m, 2H, γH's), 3.77 and 3.80 (2 s, 6H, methoxyls), 4.14 (m, 1H, H_β), 4.93 (d, J = 4.9 Hz, 1H, H_α), 6.09 (s, 1H, phenolic OH), 6.8–7.1 (m, 7H, aromatics)

^{13}C NMR (15.0 MHz, $CDCl_3$) δ 56.1 (methoxyls), 61.1 (Cγ), 73.1 (C_α), 87.1 (C_β); 132.5, 109.4, 147.1, 145.6, 114.7, 119.5 (C_1–C_6, respectively); 151.1, 147.5, 112.6, 124.2, 121.9, 120.8 (C_1'–C_6', respectively)

Triacetate of 2a

^{1}H NMR (270 MHz, $CDCl_3$) δ 2.02, 2.09, 2.28 (3 s, 9H, acetate methyls), 3.77 and 3.80 (2 s, 6H, methoxyls); ABMX pattern, A = $H\gamma_1$, B = $H\gamma_2$, M = H_β, X = H_α; ν_A = 4.26, ν_B = 4.46, ν_M = 4.67, ν_X = 6.085, J_{AB} = 11.95 Hz, J_{AM} = 4.02 Hz, J_{BM} = 5.72 Hz, J_{MX} = 5.52 Hz; 6.8–7.1 (m, 7H, aromatics)

^{13}C NMR (15.0 MHz, $CDCl_3$) δ 20.5, 20.5, 20.9 (acetate methyls), 55.8 and 55.9 (methoxyls), 62.6 (Cγ), 73.9 (C_α), 80.1 (C_β).

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